

EvolChip - Prediction of Antimicrobial Resistance

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Objectives

The significant increase of antibiotic-resistant bacteria represents one of the greatest medical challenges worldwide.

The EvolChip method enables the continuous observation of the evolutive adaptation of pathogens. Thus, an immediate prediction of the current and future effectiveness of the respective antibiotic therapy can be determined.

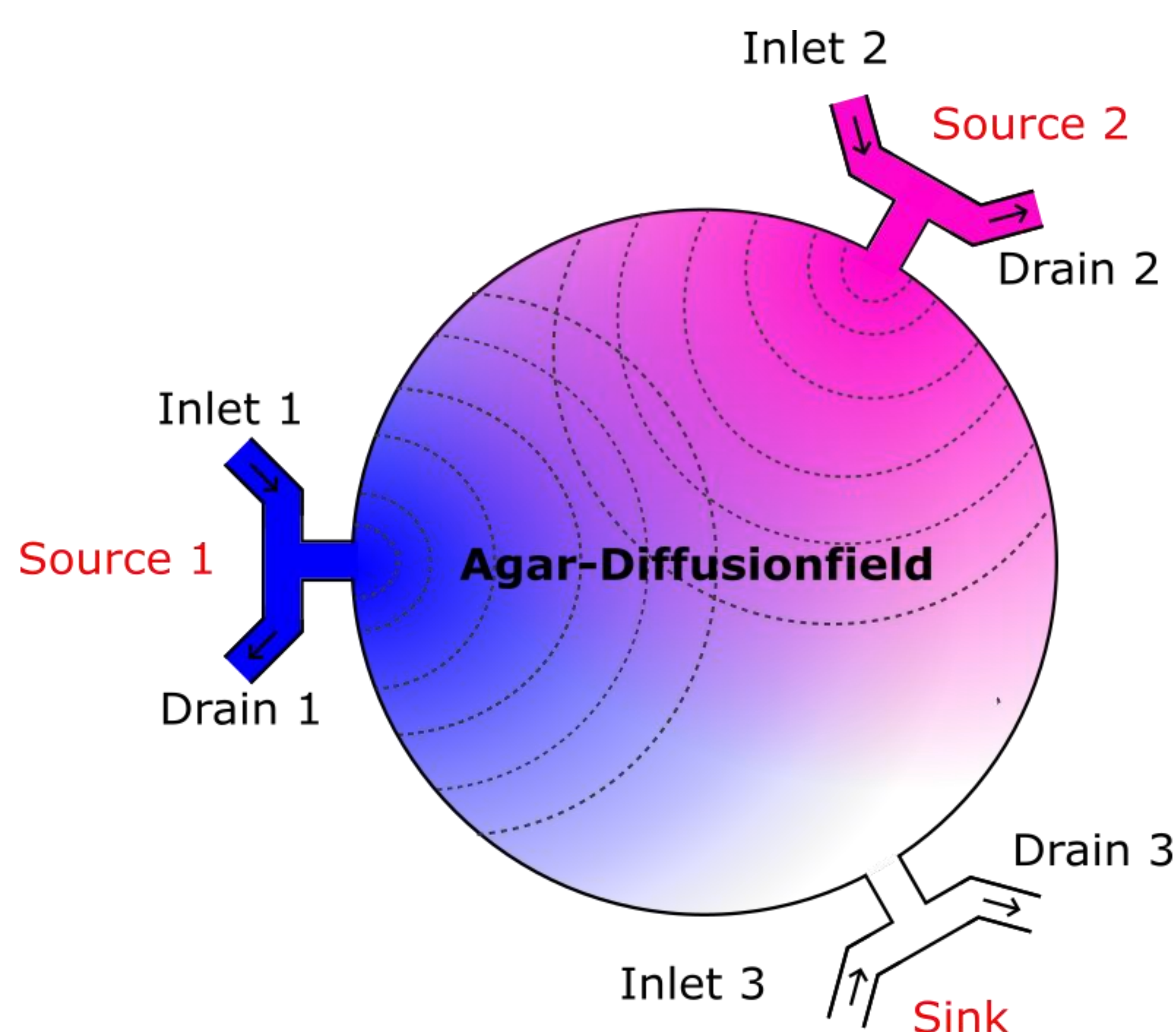


Figure 1: Concentration gradients in an agar diffusion field

Methods

The EvolChip microreactor consists of an agar plate as a diffusion and growth medium. Three membranes at different locations permit diffusion of active substances from microfluidic channels into the agar medium. Two of these channels serve as sources for different antibiotics, the third one as a sink. As a result, two overlapping gradients of antibiotics are created, with a low concentration near the sink and a high concentration close to the sources. The bacterium is inoculated on the agar culture medium and grows against the concentration gradients of the different antibiotics and their combinations in the overlapping area. A mixture of nutrient solution and antibiotics promote bacteria migration towards higher concentrated areas. The bacteria can be tracked in real-time by a green fluorescent protein gene.

Results

In preliminary experiments, the gradient profile could be characterized using fluorescent markers. Only resistant bacteria migrated towards the sources with high antibiotic concentration. The spatial distribution of bacteria enables the identification of optimal concentration ratios and mixtures of antibiotics. In addition, the speed of resistance evolution with respect to different antibiotic mixtures was determined.

Discussion

The proposed EvolChip concept showed promising results in preliminary experiments. Further geometries, growth media, and bacteria will be tested. In order to validate the method, patient strains with known treatment and resistance history will be compared to the predictions of the presented method.

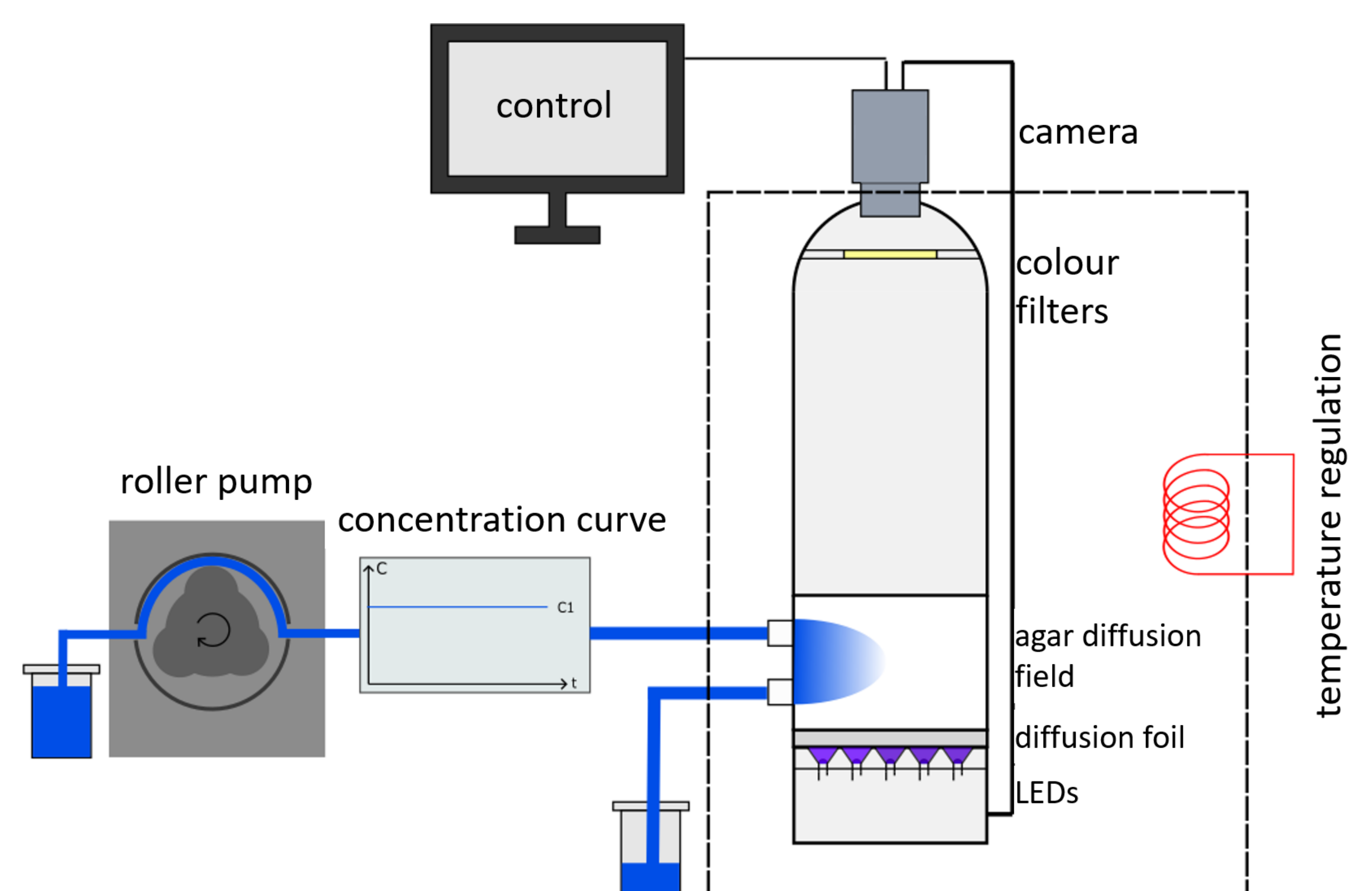


Figure 2: Experimental setup

References

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